#### (19) World Intellectual Property Organization

International Bureau



## 

(43) International Publication Date 18 December 2003 (18.12.2003)

**PCT** 

# (10) International Publication Number WO 2003/104384 A1

- (51) International Patent Classification<sup>7</sup>: C12M 1/34, 3/00, G01N 33/543, 33/487, B01J 19/00, G01N 21/01
- (21) International Application Number:

PCT/US2003/018240

(22) International Filing Date:

5 June 2003 (05.06.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/386,322

5 June 2002 (05.06.2002) U

(71) Applicant: BIOPROCESSORS CORPORATION [US/US]; 35-C Cabot Road, Woburn, MA 01801 (US).

- (72) Inventors: MILLER, Scott; 66 Gordon Street, Somerville, MA 02144 (US). LEBLANC, Sean, J.; 119 Overlook Road, Westminister, MA 01473 (US). RODGERS, Seth, T.; 68 Simpson Avenue, Somerville, MA 02144 (US). ZARUR, Andrey, J.; 30 Robinhood Road, Winchester, MA 01890 (US).
- (74) Agent: OYER, Timothy, J.; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).

- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- with international search report
- with amended claims

Date of publication of the amended claims: 26 February 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



(57) Abstract: Various aspects of the present invention relate to light-interacting components suitable for use in chips and other reactor systems. These components may include waveguides, optical fibers, light sources, photodetectors, optical elements, and the like. If waveguides are used, they may be fashioned out of any material able to transmit light to or from the reaction site. The chip may contain a reaction site having a volume of less than about 1 ml. In some embodiments, the chip may be constructed in such a way as to be able to support a living cell. The chip may be used for imaging or analysis, or the chip may be used to facilitate a chemical or biological reaction, which may be light-sensitive or light-activated in certain cases. Other facilitated reactions may include the production or consumption of a chemical or biological species. In some embodiments, the chip may include more than one component or component type, or more than one reaction site.





#### AMENDED CLAIMS

[received by the International Bureau on 22 December 2003 (22.12.03); original claims 1-96 replaced by amended claims 1-124 (9 pages)]

- 46 -

1. An apparatus, comprising:

a chip comprising a predetermined reaction site having a volume of less than about 1 ml, the predetermined reaction site constructed and arranged to maintain at least one living cell at the site, the site being suitable for cell culture; and

the site being transparent so that the site is optically accessible.

- 2. The apparatus of claim 1, wherein the chip is transparent.
- 3. The apparatus of claim 1, comprising a plurality of reaction sites.
- 4. The apparatus of claim 1, wherein the predetermined reaction site has a volume of less than about 500 microliters.
- 5. The apparatus of claim 1, wherein the predetermined reaction site has a volume of less than about 100 microliters.
- 6. The apparatus of claim 1, wherein the predetermined reaction site has a volume of less than about 10 microliters.
- 7. The apparatus of claim 1, wherein the predetermined reaction site has a volume of less than about 1 microliter.
- 8. The apparatus of claim 1, wherein the predetermined reaction site has a maximum dimension of less than about 1 cm.
- 9. The apparatus of claim 1, wherein the predetermined reaction site has a maximum dimension of less than about 1 mm.
- 10. The apparatus of claim 1, wherein the predetermined reaction site has a maximum dimension of less than about 100 micrometers.

#### 43. An apparatus, comprising:

a chip comprising a predetermined reaction site having at least one substantially hydrophobic surface and a volume of less than about 1 ml, the site being suitable for cell culture; and

the site being transparent so that the site is optically accessible.

#### 44. An apparatus, comprising:

a chip comprising a predetermined reaction site having at least one substantially hydrophilic surface and a volume of less than about 1 ml, the site being suitable for cell culture; and

the site being transparent so that the site is optically accessible.

#### 45. An apparatus, comprising:

a chip comprising a predetermined reaction site having at least one substantially cytophilic surface and a volume of less than about 1 ml, the site being suitable for cell culture; and

the site being transparent so that the site is optically accessible.

#### 46. An apparatus, comprising:

a chip comprising a predetermined reaction site having at least one substantially cytophobic surface and a volume of less than about 1 ml, the site being suitable for cell culture; and

the site being transparent so that the site is optically accessible.

#### 47. An apparatus, comprising:

a chip comprising a predetermined reaction site having a volume of less than about 1 ml, the predetermined reaction site constructed and arranged to maintain at least one living cell at the site and being suitable for cell culture; and

a photodetector in optical communication with the predetermined reaction site.

48. The apparatus of claim 47, wherein the photodetector is able to detect the presence of a cell at the predetermined reaction site.

- 58. The method of claim 56, wherein the electromagnetic radiation comprises visible light.
- 59. The method of claim 58, wherein the electromagnetic radiation consists essentially of visible light.
- 60. The method of claim 56, further comprising the step of determining a property of the interaction based on the measuring step.
- The method of claim 56, wherein the measuring step comprises determining the optical density of the altered light.
- 62. The method of claim 56, wherein the interaction comprises fluorescence.
- 63. The method of claim 56, wherein the interaction comprises light scattering.
- 64. The method of claim 56, wherein the electromagnetic radiation is substantially monochromatic.
- 65. The method of claim 56, wherein the material comprises a cell.
- 66. The method of claim 56, wherein the electromagnetic radiation has a wavelength of between about 350 nm and about 10,000 nm.
- 67. A method, comprising:

providing a predetermined reaction site having a volume of less than about 1 ml, the predetermined reaction site constructed and arranged to maintain at least one living cell at the site and being suitable for cell culture; and

optically causing a biological change in a biological material located at the predetermined reaction site.

68. The method of claim 67, wherein the biological material comprises a cell.

#### 78. An apparatus, comprising:

a chip comprising a predetermined reaction site having a volume of less than about 1 ml, the predetermined reaction site constructed and arranged to maintain at least one living cell at the site and being suitable for cell culture; and

a filter able to filter light entering or exiting the predetermined reaction site, wherein the filter is integrally connected to the chip.

#### 79. An apparatus, comprising:

a chip comprising a predetermined reaction site having a volume of less than about 1 ml, the predetermined reaction site constructed and arranged to maintain at least one living cell at the site and being suitable for cell culture; and

a light-interacting component integrally connected to the predetermined reaction site.

#### 80. An apparatus, comprising:

a chip comprising a predetermined reaction site having a volume of less than about I ml, the site being suitable for cell culture; and

an actuator able to target a first cell type within the predetermined reaction site without targeting a second cell type,

#### 81. An apparatus, comprising:

a chip comprising a predetermined reaction site having an inlet, an outlet, and a volume of less than about 1 ml, the predetermined reaction site constructed and arranged to maintain at least one living cell at the site and being suitable for cell culture, wherein the chip is substantially transparent.

#### 82. A method, comprising:

providing a chip comprising a predetermined reaction site having an inlet, an outlet, and a volume of less than about 1 ml, the predetermined reaction site constructed and arranged to maintain at least one living cell at the site and being suitable for cell culture; and

optically addressing the predetermined reaction site.

- 93. The apparatus of claim 89, wherein the silicon-based material comprises a carbide.
- 94. The apparatus of claim 89, wherein the silicon-based material comprises a nitride.
- 95. The apparatus of claim 89, wherein the silicon-based material comprises an oxide.
- 96. The apparatus of claim 87, wherein the waveguide comprises a polymer.
- 97. The apparatus of claim 96, wherein the waveguide consists essentially of the polymer.
- 98. The apparatus of claim 96, wherein the waveguide comprises polystyrene.
- 99. The apparatus of claim 96, wherein the waveguide comprises polyacrylate.
- 100. The apparatus of claim 96, wherein the waveguide comprises polymethacrylate.
- 101. The apparatus of claim 96, wherein the waveguide comprises polycarbonate.
- 102. The apparatus of claim 96, wherein the waveguide comprises polyimide.
- 103. The apparatus of claim 96, wherein the waveguide comprises polyvinylidene fluoride.
- 104. The apparatus of claim 96, wherein the waveguide comprises polyethylene.
- 105. The apparatus of claim 96, wherein the waveguide comprises polypropylene.
- 106. The apparatus of claim 96, wherein the waveguide comprises polyolefin.
- 107. The apparatus of claim 96, wherein the polymer is fluorinated.

a milled waveguide in optical communication with the predetermined reaction site.

#### 114. An apparatus, comprising:

a chip comprising a predetermined reaction site having a volume of less than about 1 ml, the site being suitable for cell culture; and

a machined waveguide in optical communication with the predetermined reaction site.

#### 115. An apparatus, comprising:

a chip comprising a predetermined reaction site having a volume of less than about 1 ml, the predetermined reaction site constructed and arranged to maintain at least one living cell at the site and being suitable for cell culture; and

an optical element in optical communication with the predetermined reaction site.

- 116. The apparatus of claim 115, wherein the optical element is integrally connected to the apparatus.
- 117. The apparatus of claim 115, wherein optical element is a diffraction grating.
- 118. The apparatus of claim 115, wherein the optical element is a lens.
- 119. The apparatus of claim 118, wherein the lens is a diverging lens.
- 120. The apparatus of claim 118, wherein the lens comprises a graded index material.
- 121. The apparatus of claim 115, wherein the optical element is constructed and arranged to focus light on a waveguide.
- 122. The apparatus of claim 115, wherein the optical element is constructed and arranged to focus light on a point located within the predetermined reaction site.

# This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

### **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

☐ BLACK BORDERS
IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
☐ FADED TEXT OR DRAWING
BLURRED OR ILLEGIBLE TEXT OR DRAWING
☐ SKEWED/SLANTED IMAGES
☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
☐ GRAY SCALE DOCUMENTS
LINES OR MARKS ON ORIGINAL DOCUMENT
☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
OTHER:

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.